

NOTES

OBSTRUCTIVE LUNG DISEASE

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- Obstruction of airflow from lungs
- Increased resistance to airflow → air-trapping
- Classifications
 - Narrowing of lumen wall (e.g. asthma, chronic bronchitis)
 - Increasing pressure external to airway/loss of lung parenchyma (e.g. emphysema)
 - Obstruction of airway lumen (e.g. bronchiectasis, chronic bronchitis)

COMPLICATIONS

- Cor pulmonale, right ventricular hypertrophy

SIGNS & SYMPTOMS

- Cough, thick mucus, dyspnea, wheezing

DIAGNOSIS

DIAGNOSTIC IMAGING

Chest X-ray/CT scan

LAB RESULTS

- Sputum culture
- Arterial blood gas (ABGs)

OTHER DIAGNOSTICS

Spirometry/pulmonary function test (PFTs)

- Tidal volume (TV)
 - Volume of air inspired, expired during quiet breathing
- Residual volume (RV)
 - Volume of air left in lung after maximal expiration
- Forced vital capacity (FVC)
 - Maximum volume of air that can be expired after maximal inspiratory effort
- Forced expiratory volume (FEV)
 - Volume of air forcibly exhaled per unit of time
- Peak expiratory flow rate (PEFR)
 - During FEV, maximum flow of expiration
- Functional residual capacity (FRC)
 - Volume of air left in lungs after quiet expiration

TREATMENT

- See individual diseases

VISIT...

LANZAROTE
Caliente.COM

ALPHA 1-ANTITRYPSIN (A1AT) DEFICIENCY

osms.it/a1at-deficiency

PATHOLOGY & CAUSES

- Autosomal dominant (codominant) genetic disorder
 - Decreased production/absence of A1AT → overaction of proteases → damaged alveoli → damaged lungs, liver
- Lungs
 - Damaged alveoli inflammation → neutrophils secrete elastase → absence of/decreased A1AT → elastase overacts, inflames → increased breakdown of elastin → **alveoli lose elasticity, integrity** → **chronic obstructive pulmonary disease (COPD)**
- Liver
 - Genetic mutation → **misfolded A1AT build up** in endoplasmic reticulum of hepatocytes → kill hepatocytes → **cirrhosis**

CAUSES

- Smoking
 - **Earlier onset of COPD** in individuals with A1AT deficiency
- Genetics
 - Serine protease inhibitor, clade A, member 1 (SERPINA1) encodes A1AT protein, located on long arm of chromosome 14
- Pi*M
 - Normal allele
- Pi*Z (most common)
 - Mutated/diseased allele
 - **Misfolded A1AT proteins aggregate** → **stick in endoplasmic reticulum of hepatocytes** → kill hepatocytes
- PiMZ
 - Heterozygous (one normal allele, one diseased allele)
 - Mutated gene contributes 10% normal

amounts A1AT proteins

- Heterozygous individuals have 60% normal levels (enough to protect lungs in non-smokers)
- Increased risk of lung/liver disease
- PiZZ
 - Homozygous
 - Individuals only have 15–20% normal levels
 - Much higher risk of lung/liver disease
 - Can live without lung/liver disease if environmental exposures minimal
 - Infants can develop liver failure during first years of life
 - Individuals with no production of A1AT = no liver disease

COMPLICATIONS

- COPD (emphysema, bronchiectasis, chronic bronchitis), hepatocellular carcinoma, liver cirrhosis, chronic hepatitis

SIGNS & SYMPTOMS

- **COPD**: shortness of breath, wheezing, mucus production, chronic cough
- **Liver damage, cirrhosis, impaired liver function**: inability to make coagulation factors, hepatic encephalopathy, portal hypertension, esophageal varices, jaundice, hepatocellular carcinoma

DIAGNOSIS

DIAGNOSTIC IMAGING

Liver ultrasound

Chest X-ray/CT scan

- Hyperinflated/damaged lungs, basilar emphysema, panlobular emphysema
 - **Smoking:** apically distributed emphysema

LAB RESULTS

- Serum A1AT levels
- Family history, genetic testing
- Liver biopsy

OTHER DIAGNOSTICS

- PFT
 - Measure rate air exits lungs
- Periodic acid-Schiff (PAS)
 - Diastase-resistant pink globules in liver biopsy
 - Stains A1AT pink

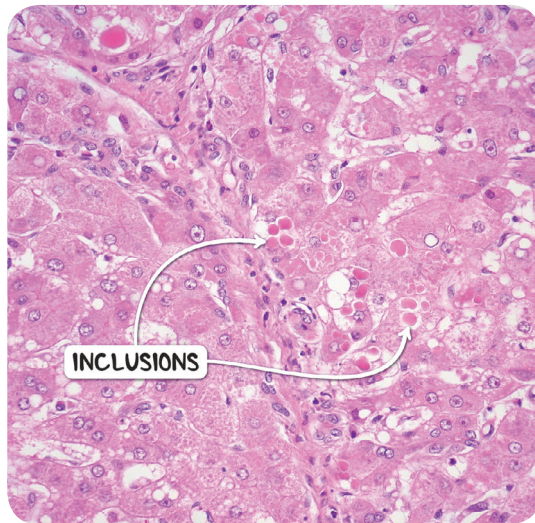


Figure 126.1 The histological appearance of the liver in an individual with alpha 1-antitrypsin deficiency. There are globular inclusions within periportal hepatocytes.

TREATMENT

MEDICATIONS

- Augmentation therapy
 - Intravenous (IV) infusions of A1AT protein from plasma donors
 - Not curative, only slows progression
- Inhalers, supplemental oxygen
 - COPD
- Lactulose
 - Prevent hepatic encephalopathy
 - For liver cirrhosis

SURGERY

- Liver transplant
 - Esp. homozygous infants, liver failure during first years
- Lung transplant

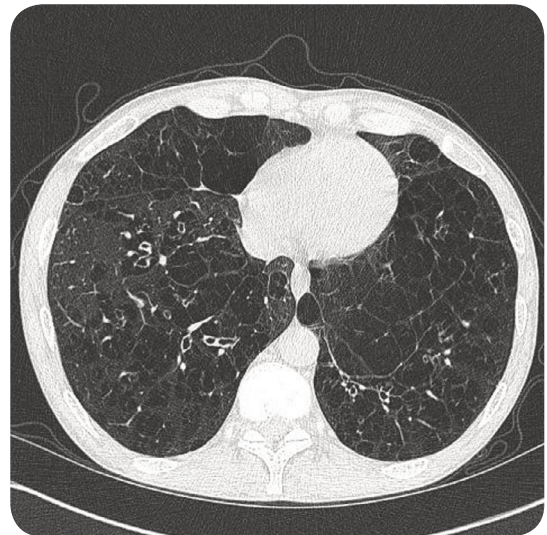


Figure 126.2 A CT scan of the chest in the axial plane demonstrating panlobular emphysema as a consequence of alpha 1-antitrypsin deficiency.

ASTHMA

osms.it/asthma

PATHOLOGY & CAUSES

- Hyperresponsiveness disorder, reversible airflow obstruction
- Chronic inflammation, narrowing of airways
- Acute (Type 1 hypersensitivity reaction)
 - Initial sensitization to allergen → production of cluster of differentiation 4 (CD4), T helper 2 (Th2) cells → release interleukin 4 (IL4), interleukin 5 (IL5) → environmental trigger → eosinophils, mast cells release inflammatory mediators in bronchial walls (e.g. histamine, leukotrienes) → degradation of lipids, proteins, nucleic acids → tissue destruction → strong inflammatory reaction in bronchiolar walls → smooth muscle of bronchioles spasm, mucus in narrow airways increases → difficulty breathing
 - Vasodilation of pulmonary vasculature, increased capillary permeability → edema
 - Increased mucus production by goblet cells → impaired mucociliary function
- Chronic inflammation → scarring, fibrosis → thickening of epithelial basement membrane → permanently narrows airway
- Th2 cells release IL5 → attract, activate eosinophils
- Neutrophils release cytokines
 - Interleukin 8 (IL8)
 - More severe for individuals with neutrophilic asthma
- Triggers
 - Air pollution, cigarette smoke, dust, pet dander, cockroaches, mold, pollen, medications (e.g. aspirin, beta-blockers)
- Individuals with atopic family history to allergies
- Atopic triad
 - Asthma, atopic dermatitis, allergic rhinitis

Intrinsic

- Nonimmune
- Viral infections, stress, exercise, smoking

SIGNS & SYMPTOMS

- Coughing, chest tightness, dyspnea, difficulty breathing, wheezing, whistling during expiration
- Curschmann spirals in sputum
 - Spiral-shaped mucus plugs
 - Casts from small bronchi
 - Blocks air exchange, inhaled medications from reaching inflammation
- Charcot-Leyden crystals in sputum
 - Needle-shaped, formed from breakdown of eosinophils

DIAGNOSIS

OTHER DIAGNOSTICS

- Trigger test, spirometry, peak air flow
- Classifications based on frequency of symptoms (esp. night/morning), forced expiratory volume in one second (FEV1), PEF, frequency of medication use (intermittent, mild persistent, moderate persistent, severe persistent)

TREATMENT

OTHER INTERVENTIONS

- No cure; treatments manage symptoms, prevent asthma attack
- Avoid triggers

TYPES

Extrinsic

- Type 1 hypersensitivity reaction triggered by extrinsic allergens (e.g. dust, mold)

PHARMACOLOGICAL MANAGEMENT OF ASTHMA

		TREATMENTS
STEP 1	Intermittent asthma	Preferred treatments: inhaled short-acting beta2-agonist (SABA) as needed (e.g. albuterol)
STEP 2	Persistent asthma	Preferred treatments: low-dose inhaled corticosteroid (ICS) (e.g. fluticasone) Alternative treatments: Cromolyn, leukotriene receptor antagonist (LTRA) (e.g. montelukast) or theophylline
STEP 3		Preferred treatments: low-dose inhaled corticosteroid (ICS) plus inhaled long-acting beta2-agonist (LABA)/ medium-dose inhaled corticosteroid (ICS) Alternative treatments: Low-dose inhaled corticosteroid (ICS) plus leukotriene receptor antagonist (LTRA)/ theophylline/ zileuton
STEP 4		Preferred treatments: medium-dose inhaled corticosteroid (ICS) plus inhaled long-acting beta2-agonist (LABA) (e.g. salmeterol) Alternative treatments: medium-dose inhaled corticosteroid (ICS) plus leukotriene receptor antagonist (LTRA)/ theophylline/ zileuton
STEP 5		Preferred treatments: high-dose inhaled corticosteroid (ICS) plus inhaled long-acting beta2-agonist (LABA), consider omalizumab for allergies
STEP 6		Preferred treatments: high-dose inhaled corticosteroid (ICS) plus inhaled long-acting beta2-agonist (LABA) plus oral corticosteroids, consider omalizumab for allergies

CLINICAL FEATURES OF ASTHMA VS. CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

ASTHMA	COPD
Intermittent airflow obstruction	Progressively worsening airflow obstruction
Improved with bronchodilators and steroids	More permanent, less reversibility
Cellular inflammation (eosinophils, mast cells, t-cells)	Cellular inflammation (neutrophils, macrophages)
Airway remodeling	Emphysema frequent
	More common in > 50 year olds

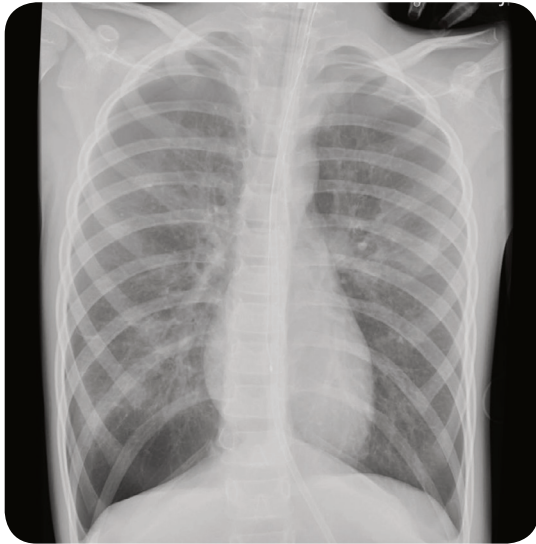


Figure 126.3 A chest radiograph demonstrating hyperinflation in an individual with chronic asthma. There is a pneumothorax in the right lower zone.

BRONCHIECTASIS

osms.it/bronchiectasis

PATHOLOGY & CAUSES

- **Chronic inflammation** → permanent dilation of bronchi, bronchioles → **destruction of airways**
 - Damage to mucociliary “elevator” → mucus, bacteria accumulates

CAUSES

Chronic inflammation

- Primary ciliary dyskinesia
 - Absence of dynein arm in cilia → cilia move abnormally → mucus stuck in airways → bacteria in mucus multiply → pneumonia → chronic inflammation
- Cystic fibrosis (most common)
 - Mucus too sticky → hard for cilia to sweep → mucus accumulates → recurrent pneumonias → chronic inflammation, infection

Airway obstruction

- E.g. tumor inside/outside airway, lodged foreign object
- Blockage prevents mucociliary escalator from clearing mucus → recurrent pneumonias → chronic inflammation

Infections

- E.g. aspergillosis, tuberculosis, adenovirus, *Haemophilus influenzae*, *Staphylococcus aureus*; hypersensitivity response → inflammation
 - Chronic inflammation → immune cells, cytokines damage cilia, elastin fibers → airways dilated, clogged with mucus → fibroblasts deposit collagen → loss of elastin, buildup of collagen → lungs less elastic → more difficult for air to move smoothly → lung function declines → hypoxia → pulmonary arterioles constrict to divert blood away from damaged areas of lung → increased

pulmonary vascular resistance →
right ventricular hypertrophy → cor
pulmonale → inflammation of pleura

SIGNS & SYMPTOMS

- Wheezing, productive cough, foul smelling mucus, dyspnea, hemoptysis, recurrent/persistent pneumonia, basilar crackles
- Long term hypoxia
 - Digital clubbing

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan

- Dilated bronchi/bronchioles

Chest X-ray

- Increased bronchial markings at lung periphery

LAB RESULTS

- Sputum culture
- Genetic testing

OTHER DIAGNOSTICS

- Spirometry
 - FEV1 decreased, FEV1/FVC ratio decreased
- Sweat test

TREATMENT

MEDICATIONS

- Bronchodilators; beta-2 agonists (e.g. albuterol)
- Inhaled corticosteroids (e.g. fluticasone)
- Antibiotics
 - Recurrent pneumonias

OTHER INTERVENTIONS

- Percussion, postural drainage
 - Recurrent pneumonias
- Pulmonary hygiene
- Adequate hydration

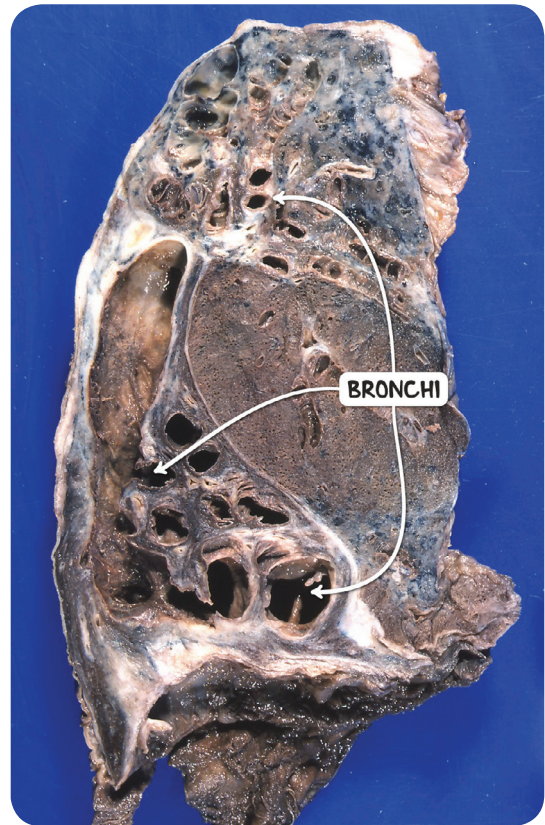


Figure 126.4 The gross pathological appearance of the lungs in a case of severe bronchiectasis.

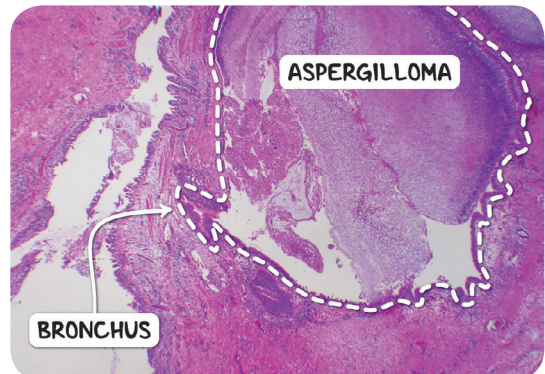


Figure 126.5 The histological appearance of bronchiectasis complicated by fungal colonisation. There is a heavily dilated bronchus containing an aggregation of fungus known as an aspergilloma.

CHRONIC BRONCHITIS

osms.it/chronic-bronchitis

PATHOLOGY & CAUSES

- Preventable, progressive pulmonary disease
 - Chronic airway inflammation, limited airflow
 - Bronchial tubes in lungs inflame → productive cough
- Subset of COPD
- Exposure to irritants → hypertrophy/hyperplasia of bronchial mucous glands, goblet cells in bronchioles, cilia less mobile → increased mucus production, less movement → mucus plugs → obstruction in bronchioles → air-trapping → productive cough
- Blocked airflow, air-trapping → increased partial pressure of CO_2 in lungs → less O_2 reaches blood → cyanosis (if severe); individuals referred to as “blue bloaters”

RISK FACTORS

- Smoking (primary cause), cystic fibrosis, sulfur, nitrogen dioxide, dust, silica, family history, genetic predisposition

COMPLICATIONS

- Pulmonary hypertension, increased workload of right ventricle, cor pulmonale, infections distal to mucus blockages, fibrosis of terminal bronchioles, compensatory polycythemia

SIGNS & SYMPTOMS

- Wheezing (due to mucus, narrow airway), crackles/rales (small airways pop open during air movement due to narrow passageway)
- Hypoxemia, hypercapnia (due to mucus plugs blocking air flow) → cyanosis → tissue hypoxia

DIAGNOSIS

DIAGNOSTIC IMAGING

Chest X-ray

- Large, horizontal heart, increased bronchial markings

LAB RESULTS

- ABGs
 - Respiratory acidosis (arterial $\text{PCO}_2 > 45\text{mmHg}$, bicarbonate $> 30\text{mEq/L}$)

OTHER DIAGNOSTICS

- Productive, mucinous cough
 - At least **three months over two consecutive years**
- PFTs
 - Increased TLC, air-trapping; decreased FVC1/FVC ratio
- Postmortem measurement
 - Reid index (measure ratio of thickness of bronchial mucinous glands, total thickness of airway, epithelium to cartilage)
 - $> 40\%$ (due to hyperplasia, hypertrophy of glands)

TREATMENT

MEDICATIONS

- Supplemental oxygen, bronchodilators, inhaled steroids, antibiotics
 - Manage symptoms
- Prophylactic vaccination against influenza, *Streptococcus pneumoniae* (S. pneumoniae)

OTHER INTERVENTIONS

- Smoking cessation, pulmonary rehabilitation

CYSTIC FIBROSIS (CF)

osms.it/cystic-fibrosis

PATHOLOGY & CAUSES

- Autosomal-recessive multisystem disorder
 - Affects lungs, digestive system, reproductive system, sweat glands
- Caused by *CFTR* gene defect (located on long arm of chromosome 7)
 - Encodes cyclic adenosine monophosphate-regulated chloride channel cystic fibrosis transmembrane conductance regulator (CFTR)
 - Various mutations: including lack of protein production; protein trafficking defect, degradation within cellular endoplasmic reticulum, Golgi body
- Genetic defect → impaired sodium, chloride transport across epithelial cell surface → thick, tenacious secretions
 - Classic triad: ↑ sweat chloride levels, chronic sinopulmonary disease, pancreatic insufficiency
- Bronchi effects
 - Goblet cell hyperplasia, submucosal gland hypertrophy → production of viscous mucus, mucus plugging → airway inflammation → elastase released from neutrophils → tissue destruction → ↑ thickness of airway walls, bronchiectatic cysts, ventilation-perfusion mismatch → hypoxemia

RISK FACTORS

- Family CF history; especially carrier parents
- ↑ incidence in white people of Northern, Central European descent

COMPLICATIONS

- Chronic respiratory tract infections
 - Common bacteria: *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Haemophilus influenzae* (especially younger children)
 - Invasive fungal disease may occur → allergic bronchopulmonary aspergillosis

(ABPA)

- Sinusitis
 - Related to chronic inflammation
- Significant hemoptysis
 - Related to enlarged, tortuous bronchial arteries
- Bronchiectasis
 - Due to mucus plugging
- Pneumothorax
 - Related to ruptured emphysematous bullae
- Secondary pulmonary hypertension
 - Related to small pulmonary artery hypertrophy
- Nasal polyps
 - Related to chronic inflammation
- Respiratory failure
- Non-pulmonary complications
 - Cirrhosis; gallstones; pancreatitis; heat exhaustion, dehydration; hypochloremic alkalosis (excessive salt-loss in sweat); rectal prolapse; infertility (azoospermia); fat-soluble vitamin deficiency; anemia; nail clubbing

SIGNS & SYMPTOMS

- Highly variable presentation
 - Related to specific mutation, gene penetrance, environmental factors
- Specific pulmonary manifestations
 - Chronic, productive cough; dyspnea; ↑ anterior-posterior chest diameter; digital clubbing; basilar crackle; expiratory wheeze; generalized hyperresonance

DIAGNOSIS

DIAGNOSTIC IMAGING

Prenatal ultrasound

- May detect hyperechogenic bowel, meconium peritonitis

Chest X-ray

- Hyperinflation, air trapping, atelectasis, flattened diaphragm, peribronchial thickening, bronchovascular markings, peribronchial cuffing, parallel lines (related thickened bronchial walls—"tram tracks")

CT scan

- Inspissated bronchial secretions; detects degree of bronchiectasis

LAB RESULTS

- Genetic testing
- *CFTR* mutation identification
- **Sweat chloride test**
 - ↑ sweat chloride concentration
 - Pilocarpine administered → stimulate sweat; collected, analyzed for chloride content

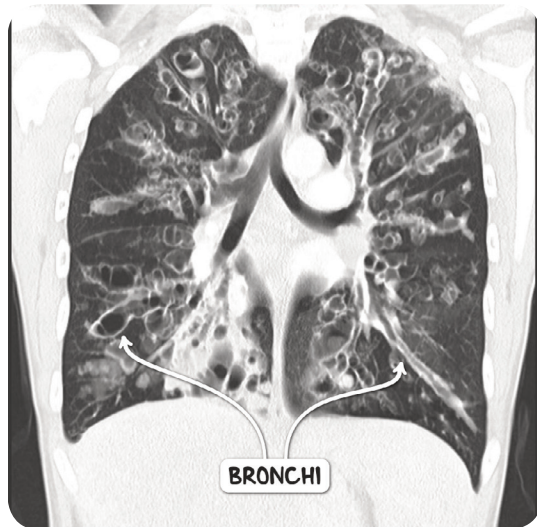


Figure 126.7 A CT scan of the chest in the coronal plane demonstrating bilateral widespread bronchiectasis in a twenty five year old female with cystic fibrosis.

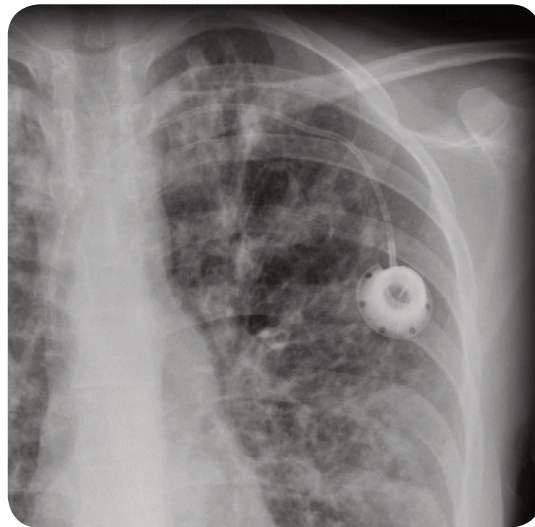


Figure 126.6 A plain chest radiograph demonstrating tram-track opacities and ring shadows in an individual with cystic fibrosis. They are particularly well demonstrated in the left upper zone.

OTHER DIAGNOSTICS

- **Newborn screening**
 - Detects CF in neonatal period; initiate early intervention
- Pulmonary function tests
 - ↓ FEV1 FEV1/FVC
 - ↑ residual volume to total lung capacity (RV/TLC) ratio
 - ↓ total lung capacity
 - ↓ vital capacity

TREATMENT

MEDICATIONS

- CFTR modulators
- Medications to clear respiratory secretions; inhaled hypertonic saline
- **Anti-inflammatory medications** (e.g. glucocorticoids)
- Antibiotics
 - Infections
- **Bronchodilators**
 - ↓ airflow obstruction
- Prevention
 - Annual influenza vaccine; pneumococcal vaccine

SURGERY

- Lung transplantation
- Respiratory support
 - Respiratory failure → invasive ventilation

OTHER INTERVENTIONS

- Address complications
- Chest physiotherapy
 - Mobilize retained secretions
- Respiratory support
 - Supplemental oxygen
 - Positive-pressure ventilation

EMPHYSEMA

osms.it/emphysema

PATHOLOGY & CAUSES

- COPD subset
 - Exposure to irritants → degrades elastin in alveoli, airways → air-trapping, poor gas exchange.
- Irritants (e.g. cigarette smoke) → attraction of inflammatory cells → release leukotrienes, chemical mediators (e.g. B4; IL8; TNF alpha/proteases, elastases/collagenases) → destroy collagen, elastin → lose elasticity → low pressure during expiration pulls walls of alveoli inward → collapse → air-trapping distal to collapse → septa breaks down → neighboring alveoli coalesce into larger air spaces → decreased surface area available for gas exchange
 - Loss of elastin → lungs more compliant (lungs expand, hold air)
 - Alveolar air sacs permanently enlarge, lose elasticity → exhaling difficult

Paraseptal emphysema

- Distal alveoli most affected
 - Lung tissue on periphery of lobules near interlobular septa
 - Ballooned alveoli on lung surface rupture → pneumothorax

CAUSES

- Smoking, A1AT deficiency

COMPLICATIONS

- Hypoxic vasoconstriction → cor pulmonale
 - Poor gas exchange → vessels vasoconstrict to shunt blood to better gas exchange → pulmonary hypertension → increased workload for right heart → right ventricular hypertrophy → cor pulmonale
- Hypoxemia
- Pneumothorax

TYPES

Centriacinar/centrilobular emphysema

- Most common
- Damage to central/proximal alveoli of acinus sparing distal alveoli
 - Individuals who smoke (irritants can't reach distal alveoli); upper lobes of lungs

Panacinar emphysema

- Entire acinus uniformly affected
 - A1AT deficiency; lower lobes of lungs

SIGNS & SYMPTOMS

- Barrel chest (air-trapping, hyperinflation of lungs), apparent respiratory distress with use of accessory muscles, tripod positioning, weight loss, exhaling slowly through pursed lips ("pink puffers"), hyperventilation
- Pursed lips increases pressure in airway → keeps airway from collapsing → weight loss
- Dyspnea, cough (with less sputum)

DIAGNOSIS

DIAGNOSTIC IMAGING

Chest X-ray

- Increased anterior-posterior diameter, flattened diaphragm, increased lung field lucency (air-trapping)

OTHER DIAGNOSTICS

- Increased TLC
- FVC decreased (esp. FEV1)

TREATMENT

MEDICATIONS

- Bronchodilators
- Inhaled steroids
- Combination inhalers
 - Bronchodilators + inhaled steroids
- Oral steroids
 - Adverse effects: oral candidiasis, weight gain, diabetes, osteoporosis
- Antibiotics (e.g. azithromycin prevents exacerbations)
- Supplemental oxygen

SURGERY

- Lung volume reduction
 - Removal of areas of damaged lung tissue to create extra space in chest cavity for healthy lung tissue to expand
 - Can improve quality of life and prolong survival
- Lung transplant
- Bullectomy
 - Removal of bullae (large air spaces) to improve air flow

OTHER INTERVENTIONS

- Pulmonary rehabilitation program
 - Customized education plan consisting of exercising training, nutrition advice, and lifestyle counseling

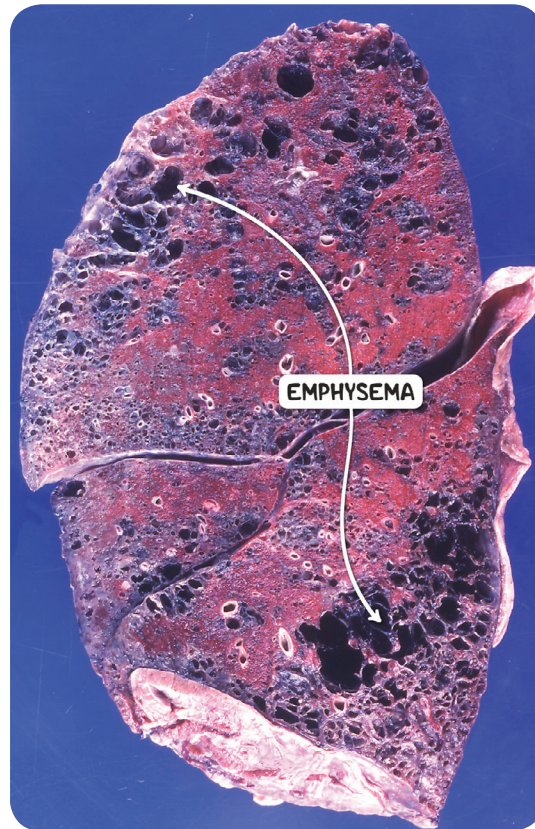


Figure 126.8 The gross pathological appearance of emphysema. There are numerous dilated airspaces in a peripheral distribution.

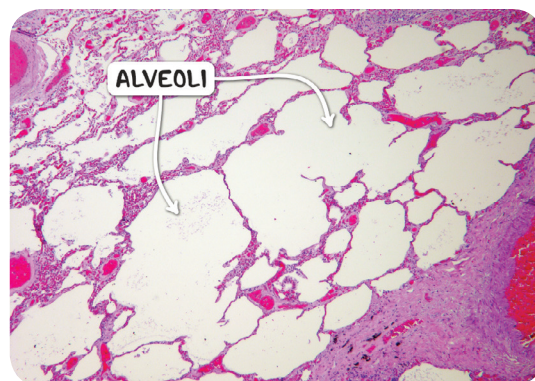


Figure 126.9 The histological appearance of emphysema. There are numerous hyperexpanded alveoli.

COMPARISON OF SIGNS & SYMPTOMS: EMPHYSEMA VS. CHRONIC BRONCHITIS

	EMPHYSEMA	CHRONIC BRONCHITIS
pH	Normal to ↑	↓
PaCO ₂	Normal to ↓	↑
PaO ₂	↓	↓
CYANOSIS	Absent	Present
HYPOXEMIA	Presents late	Presents early
DYSPNEA	Presents early	Presents late
APPEARANCE	Thin, leans forward when sitting, barrel chest, in apparent respiratory distress with use of accessory muscles "Pink puffer"	Overweight, cyanotic, in no apparent respiratory distress with no apparent use of accessory muscles "Blue bloater"



MNEMONIC: P vs. B

Emphysema vs. Bronchitis

EmPhysema: Pink Puffer

Chronic Bronchitis: Blue Bloater